Paper 28

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

JEFFREY M. **STAUB**,
PETER H.J. HAJDUKIEWICZ, and LARRY GILBERTSON,
Junior Party
(Patent 6,849,778,

v.

PAL **MALIGA**
and SYLVIE CORNEILLE
Senior Party
(Application 10/088,634).

Patent Interference No. 105,420
(Technology Center 1600)

**Decision - Motions - Bd. R. 125(a)**

Before McKelvey, Senior Administrative Patent Judge, and Delmendo and Lane, Administrative Patent Judges.

Lane, Administrative Patent Judge.

I. Introduction

Staub and Maliga have filed a joint motion seeking a judgment of no interference-in-fact. (Paper 27). The motion is GRANTED.

II. Findings of fact

The record supports the following findings of fact by at least a preponderance of the evidence.

1. The interference was declared on 22 February 2006. (Paper 1).

2. Junior party in the interference is Jeffrey M. Staub, Peter H.J. Hajdukiewicz, and Larry Gilbertson (Staub).

3. Staub is involved on the basis of its patent 6,849,778 ('778) , issued on 01 February 2005 from application 09/688,851, filed 16 October 2000.

4. Maliga is involved on the basis of its 10/088,634 ('634) application, filed 16 October 2002.

5. There is one Count in the interference, Count 1, which is defined as "Claim 1 of Maliga or claim 2 of Staub". (Paper 1 at 4).

6. All the claims of each party, i.e., claims 1-21 of the '634 application and claims 1-4 of the '778 patent, correspond to Count 1.

7. The parties have been accorded the following benefit for priority purposes as to Count 1:

Maliga:

PCT/US00/25930, filed 21 September 2000
US 60/211,139, filed 13 June 2000
US 60/155,007, filed 21 September 1999

Staub:

US 60/225,542, filed 16 August 2000
US 60/159,876, filed 15 October 1999

*Maliga claims*

8. Claim 1 of the involved Maliga application is as follows:

A site specific recombination method for removal of predetermined nucleic acid sequences from the plastid genome, said method comprising:

a) providing a first nucleic acid construct, said construct comprising a promoter being operably linked to a nucleic acid encoding plastid targeting transit sequence which is operably linked to a nucleic acid encoding a site specific recombinase having excision activity, said construct further comprising a first selectable marker encoding nucleic acid having plant specific 5' and 3' regulatory nucleic acid sequences;

b) providing a second DNA construct, said second construct comprising an second selectable marker encoding nucleic acid sequence which is flanked by excision sites, said second construct optionally containing a gene of interest, said second construct further comprising flanking plastid targeting nucleic acid sequences which facilitate homologous recombination into said plastid genome;

c) introducing said second DNA construct into a plant cell;

d) culturing said plant cell of step c) in the presence of a selection agent, thereby selecting for those plant cells expressing the proteins encoded by said second DNA construct;

e) introducing said first DNA construct into plant cells from step d) in the presence of a selection agent and selecting those plant cells expressing proteins encoded by said first construct, which when present said site specific recombinase acts on said excision sites, thereby removing said sequence flanked by said excision sites from said plastid genome.

9. Maliga claims 2-11 and 20 depend, directly or indirectly, from claim 1.

10. Claim 2 requires that a step of regenerating a plant occurs after step (c).

11. Claims 3 and 4 are directed to specific "first [nucleic acid] constructs".

12. Claim 5 is directed to specific site specific recombinases.

13. Claim 6 is directed to specific excision sites.

14. Claim 7 is directed to specific selection agents.

15. Claim 8 requires that the "excision of said predetermined sequences creates an expressible translational fusion protein."

16. Claim 9 requires that the "predetermined target sequence"[1] be the selectable marker encoding nucleic acid of the second [DNA] construct.

17. Claim 10 is directed to a plant generated from the method of claim 1.

18. Claim 11 is directed to a "site specific recombination system comprising the constructs of the method of claim 1."

19. Claim 20 is directed to progeny plants of the claim 10 plant.

20. Maliga claim 12 is the following independent claim:

A site specific recombination method for removal of predetermined nucleic acid sequences from a plastid genome, said method comprising:

a) providing a first nucleic acid construct, said construct comprising a regulated promoter being operably linked to a nucleic acid encoding a plastid targeting transit sequence which is operably linked to a nucleic acid encoding a site specific recombinase having excision activity, said construct optionally further comprising a first selectable marker encoding nucleic acid having plant specific 5' and 3' regulatory nucleic acid sequences;

b) providing a second DNA construct, said second construct comprising a second selectable marker encoding nucleic acid, said second construct further comprising
flanking plastid targeting nucleic acid sequences which flank a pair of excision sites, the second selectable marker encoding nucleic acid and a predetermined nucleic acid sequence from a plastid genome, wherein the excision sites flank the second selectable marker encoding nucleic aid and the predetermined nucleic acid sequence, wherein said plant targeting nucleic acid sequences facilitate homologous recombination into said plastid genome comprising said predetermined sequence targeted for deletion;

c) introducing said second DNA construct into a plant cell and allowing said homologous recombination to occur;

d) culturing a plant cell of step c) in the presence of a selection agent, thereby selecting for those plant cells expressing the proteins encoded by said second DNA construct;

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[1] This term appears to lack antecedent basis in claim 1 but we understand it to refer to the "predetermined nucleic acid sequences"

e) regenerating a plant from cells obtained in step d);

f) introducing said first DNA construct into plant cells from the plant of step e) in the presence of a selection agent and selecting those plant cells expressing proteins encoded by said first construct, which when present said site specific recombinase acts on said excision sites, thereby removing said predetermined nucleic acid sequence and said second selectable marker nucleic acid sequence from the plastid genome.

21. Claims 13-19 and 21 depend, directly or indirectly, from claim 12.

22. Claim 13 is directed to particular regulatable promoters.

23. Claim 14 is directed to particular predetermined target sequences.

24. Claim 15 is directed to certain proteins having excision activity.

25. Claim 16 is directed to certain excision sites.

26. Claim 17 is directed to certain selection agents.

27. Claim 18 is directed to a plan generated from the plant cells of step f).

28. Claim 19 is directed to a site specific recombination system comprising the claim 12 construct.

29. Claim 21 is directed to progeny of the plant obtained from the plants of claim 17.[2]

*Staub claims*

30. Claim 2 of the involved Staub patent is as follows:

The method according to claim 1, wherein said recombinase is provided to said plant cell by introducing a third recombinant DNA sequence comprising in an operably coupled 5' to 3' manner:

a transcriptional initiation region, a plastid targeting region, and a nucleic acid sequence encoding recombinase.

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[2] It appears that claim 21 should refer to claim 18 since it is claim 18, not claim 17, that is directed to a plant.

31. Claim 1 of the involved Staub patent, from which claim 2 depends, is as follows:

A method for performing multiple rounds of plastid transformations in a plant cell plastid using the same selectable marker for selection of transplastomic plants comprising:

(a) introducing into a plant cell a first recombinant DNA sequence comprising a construct capable of being integrated into the plastid genome of the plant cell, said construct comprising an expression cassette comprising a DNA sequence of interest to be expressed in the plastid and a selectable marker cassette comprising a promoter that initiates expression of an operably linked DNA sequence in a plant plastid, a DNA sequence encoding a protein that permits for the selection of a transformed plastid and a 3' transcription termination region, said selectable marker cassette flanked by a pair of compatible recombining sites arranged in parallel orientation as direct repeats, to produce a plant cell having a plastid containing said first recombinant DNA sequence;

(b) selecting for the cell containing a transformed plastid;

(c) providing a recombinase compatible to said pair of compatible recombining sites to said plant cell to permit excision of said DNA sequence encoding a protein that permits for the selection of a transformed plastid and producing excision of said DNA sequence;

(d) regenerating a transplastomic plant containing said first recombinant DNA sequence without said DNA sequence encoding a protein that permits for the selection of a transformed plastid from said plant cell;

(e) introducing into a plant cell of said transplastomic plant a second recombinant DNA sequence comprising a construct capable of being integrated into the plastid genome of the plant cell, said construct comprising a second expression cassette comprising a second DNA sequence of interest to be expressed in said plastid and second selectable marker cassette comprising a promoter that initiates expression of an operably linked DNA sequence in a plant plastid, a DNA sequence encoding the same protein as in the first recombinant DNA sequence that permits for the selection of a transformed plastid and a 3' transcription termination region, into a plant cell of said transplastomic plant obtained from said regenerated plant thereby producing a plastid having said second recombinant DNA sequence in said plant cell of said transplastomic plant; and

(f) producing a transplastomic plant having said first and second recombinant DNA sequences introduced sequentially into said plastid using the same selectable marker for the second recombinant DNA sequence as used for the selection of the first recombinant DNA sequence.

32. Staub claims 3 and 4 depend from claim 1.

33. Claim 3 further limits the DNA sequence of interest in either the first or second expression cassette.

34. Claim 4 further limits the pair of compatible recombining sites.

35. The parties argue that the involved claims of Maliga do not anticipate or render obvious the involved claims of Staub.

36. In particular, the parties argue that there are at least two steps in the methods defined by the Staub claims that are not found in the methods defined by the Maliga claims.

37. The parties argue that the methods of the Staub claims require: (1) regeneration of an intermediate plant, and (2) insertion of a second DNA of interest into the plant cell (Paper 27 at 7).

38. The parties argue that:

> Moreover, the transgenic plants generated using the respective methods are not identical in that the plants resulting from the claimed methods of Staub et al, in the '778 patent express a plurality of nucleic acids encoding sequences of interest and at least one selectable marker, whereas the Maliga claimed method provides plant cells expressing a single nucleic acid of interest without a selectable marker.

(Paper 27 at 7).

39. The parties have not directed us to any testimony to indicate the scope and content of the prior art.

40. Instead, the parties represent that they are unaware of prior art that would have rendered the Staub claims obvious in view of the Maliga claims. (Paper 27 at 8).

41. In the Form 850 (attached to Paper 1), the examiner addressed why he believed the Maliga claims would have been obvious in view of the Staub claims but not vice versa.

III. Discussion

"An interference exists if the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party and vice versa." Bd. R. 203(a). The parties argue that there is no interference since the claims of Staub are not anticipated or rendered obvious by the claims of Maliga. The parties have the burden of proof to establish that no interference exists. Bd. R. 121(b).

The parties argue that the Staub claims are patentably distinct from the Maliga claims in at least three way. In particular, the parties argue that:

(1) the Staub claims require regeneration of an intermediate plant while the Maliga claims do not,

(2) the Staub claims require insertion of a second DNA of interest into the plant cells while the Maliga claims do not, and

(3) the final plants regenerated using the methods claimed by Staub have cells expressing a plurality of nucleic acids encoding sequences of interest and a selectable marker while the Maliga claimed method provides plants having cells expressing a single nucleic acid of interest and no selectable marker.

We consider each argument below.

The generation of an intermediate plant

Each of the claimed methods of Staub and the claimed methods of Maliga call for the introduction of a first construct (which is identified as the "second DNA construct" in the Maliga claims (see step c)) into a plant cell.[3] The first construct to be introduced contain, in each of the Staub and Maliga methods, *inter alia*, a first marker sequence and a DNA of interest. The parties do not argue that the introduction of this first construct is a basis for determining that the Staub and Maliga claims are patentably distinct.

Each of the claimed methods of Staub and the claimed methods of Maliga call for the introduction of a recombinase that is effective to permit excision of the first marker sequence introduced by the first construct. The parties note that, in the Staub method, the recombinase is introduced and the first marker is removed, prior to regeneration of the intermediate plant (step (d) of Staub claim 1). (Paper 27 at 6). In contrast, in the Maliga method, the recombinase is introduced, and thus the first marker is removed( at, e.g., step(e) of Maliga claim 1), after the intermediate plant is produced.[4] According to the parties, the claims of Maliga do not anticipate or render obvious the claims of Staub since the Maliga claims do not recite a step of introducing a

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[3] We note that, in addition to its method claims, Maliga has product claims involved in the interference. Claim 10, 12, 20, and 21 are directed to plants or their progeny produced using the claimed methods. Claims 11 and 19 are directed to site specific recombination systems comprising the constructs used in the method claims. We consider the parties' arguments as also applying to these product claims.

[4] Maliga claim 1 does not recite regeneration of an intermediate plant. Maliga claim 2 requires the regeneration of a plant after the introduction of the first construct into the plant cells but before selection of the cells that express the proteins encoded by the first construct or removal of the marker sequence. Maliga claim 12 requires regeneration of a plant after selection the cells that express the proteins encoded by the first construct but prior to removal of the marker sequence.

recombinase and thus removing the first marker sequence prior to intermediate plant regeneration.

Second DNA of interest

As noted by the parties, (Paper 27 at 6-7), the Staub claims recite a step of introducing a construct containing a second DNA sequence of interest (step (e) of Staub claim 1) after the recombinase is introduced and after the first marker is removed. In contrast, the Maliga claims do not recite such a step.

The parties argue that the claims of Maliga do not anticipate or render obvious the claims of Staub since the Staub claims recite a step of introducing a second DNA of interest into the plant cells and the Maliga claims do not.

Final plant produced

The Staub and Maliga claims each call for production of a plant that results from the sequential introduction of certain genetic constructs into the plastids of plant cells. (See, e.g., Staub claim 1 at step (f) and Maliga claim 10). The parties argue that the claims of Staub call for the production of a plant having two DNA sequences of interest while the claims of Maliga do not call for the production of a plant having two DNA sequences of interest. The parties further argue that the cells of the final plants produced by the methods of Staub contain a selectable marker while the cells of the final plants produced by the Maliga methods do not.

Anticipation and obviousness

To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either expressly or inherently. *In re Schreiber*, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). The parties have demonstrated that the

claims of Maliga do not anticipate the claims of Staub. The parties argue that the methods of the Staub claims require at least two steps that are not found in the methods of the Maliga claims: (1) regeneration of an intermediate plant, and (2) insertion of a second DNA of interest into the plant cell. The parties further argue that the methods of Staub call for production of final plant products having cells containing two DNA sequences of interest and a second selectable marker in place.

While the parties have convincingly demonstrated a lack of anticipation, the proof of unobviousness provided in the motion is less compelling. An obviousness analysis requires findings regarding the scope and content of the prior art. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966). However, the parties have not directed us to any objective evidence of nonobviousness, such as testimony from one skilled in the art.[5] The standard for proving a negative (in this case that something is not obvious) is relaxed but nonetheless must be sufficiently addressed. In this case, each party has represented that it is unaware of evidence contrary to its position. Such a statement may, depending on the circumstances, be sufficient to satisfy the movant's burden of proof.

In these circumstances, we have the assurances from each party that it is unaware of prior art that would indicate that the Maliga claims would have rendered the Staub claims obvious, coupled with the record before us which does not contain sufficient information for us to determine that there would have been a reasonable expectation of successfully arriving at the Staub claimed invention in view of the Maliga

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[5] See standing order at ¶ 208.1.

claimed invention. In the particular circumstances before us, we determine that there is sufficient basis in the present record to grant the relief requested. A judgment of no interference-in-fact will be entered in a separate paper.

## IV. Order

Upon consideration of the record and for reasons given, it is

ORDERED that the Staub and Maliga joint Motion 1 for a judgment of no interference-in-fact is GRANTED.

/Fred E. McKelvey/
FRED E. MCKELVEY
Senior Administrative Patent Judge

/Romulo H. Delmendo/
ROMULO H. DELMENDO
Administrative Patent Judge

/Sally G. Lane/
SALLY G. LANE
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